PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32596A	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/08315	International filing date *(day/month/year)* 28.07.2003	Priority date *(day/month/year)* 29.07.2002
International Patent Classification (IPC) or both national classification and IPC G01N1/22		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.01.2004	27.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Filipas, A Telephone No. +49 89 2399-2255

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/08315

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-23 filed with telefax on 18.10.2004

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

☐ the description, pages:

☒ the claims, Nos.: 24,25

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-23
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-23
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, previously cited in the International Search Report:

   D1: Jian Peng et al.: 'EFFECT OF IONIC STRENGTH ON HENRY'S CONSTANTS OF VOLATILE ORGANIC COMPOUNDS' Chemosphere, Pergamon Press, Oxford, GB, vol. 36, no. 13, June 1998, pages 2731-2740, ISSN: 0045-6535

   D2: Banat F. A. et al.: 'Experimental Study of the Salt Effect in Vapor/Liquid Equilibria Using Headspace Gas Chromatography' Chemical Engineering & Technology, Weinheim, DE, vol. 22, no. 9, 1999, pages 761-765, ISSN: 0930-7516

   D3: Patent Abstracts of Japan vol. 016, no. 562 (P-1456), 3 December 1992 & JP-A-04 215062 (SHIMADZU CORP), 5 August 1992

   D4: Comberbach D. M. et al.: 'Automatic On-line Fermentation Headspace Gas Analysis Using A Computer-Controlled Gas Chromatograph' Biotechnology and Bioengineering, John Wiley & Sons, Inc., New York, US, vol. 25, no. 11, 1983, pages 2503-2518, ISSN: 0006-3592

2. The present application does not appear to meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is anticipated by each of the documents D1 (see e.g. the abstract), D2 (see e.g. the abstract), D3 (see e.g. the abstract) and D4 (see e.g. the sentence bridging pages 2512 and 2513) and is therefore not new (Article 33(2) PCT) and does not involve an inventive step (Article 33(3) PCT).

   Although the expression "ionic liquids" is currently used to define "salts with a melting temperature with a melting point below the boiling point of water" (which, by the way, does not apply to the embodiment defined in claim 9), it can also be understood in its broader sense (see e.g. the description, page 4, lines 16-17), i.e. as liquids characterized by a positively charged cation and a negatively charged anion.
   Since not only molten salts but also salt solutions fall under the scope of said broader definition, the subject-matter of claim 1 is anticipated by each of the documents D1-D4, all of which refer to the use of salt solutions in water as solvents in headspace gas chromatography, wherein a sample is dissolved or dispersed in such a salt solution and then the volatile compounds of the sample are volatilized.

It should be noted that the expression "ionic liquids such as molten salts" used in claim 1 does not restrict the meaning of ionic liquids to molten salts, but only indicates that molten salts represent an example of ionic liquids.

3. The additional feature of claim 2 is not disclosed in any of the documents cited in the International Search Report. The subject-matter of claim 2 (insofar as it can be understood in view of the clarity objection under paragraph 6.1 below) appears therefore to be new (Article 33(2) PCT).

However, the feature of claim 2 cannot be considered as involving an inventive step (Article 33(3) PCT), since it consists merely in a new use of a known material, and this use only involves the employment of the known properties of said material.

4. Claims 3-23 are dependent on claim 2 and as such also meet the requirements of the PCT with respect to novelty.

However, dependent claims 3-23 do not appear to contain any additional features which would involve an inventive step, the reasons being that said dependent claims seem to relate to mere normal options or to consequential features of the basic method of claim 2.

5. Claims 1-23 appear to satisfy the criterion of industrial applicability (Article 33(4) PCT), since the claimed invention can be used in the field of headspace gas chromatography.

6. Certain observations on the international application

6.1 Claim 2 is rendered unclear (Article 6 PCT) by its dependency on a following claim.

6.2 The amendments filed by telefax on 18.10.2004 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 19(2) PCT. The amendments concerned are those of claim 12.

It should be noted that claim 14 as initially filed, on which the new claim 12 is

apparently based, only mentions imidazolium salt, pyridinium salt, ammonium salt, phosphonium salt and sulphonium salt, and **no mixtures thereof**.

6.3 The vague and imprecise statement in the description on page 11, lines 10-12, implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

6.4 The unit "centipoise (cP)" employed on page 4, lines 30-31, is not additionally expressed in terms of the units stipulated by Rule 10.1 (a) PCT.

Claims:

1. A method of using an ionic liquid as solvent in headspace gas chromatography.

2. A method of using ionic liquids as solvents in headspace gas chromatography wherein said method comprises dissolving or dispersing a sample in at least one ionic liquid and volatilizing the volatile components of the sample.

3. The method according to Claim 1 or 2 wherein the ionic liquid has a melting point of less than 250°C.

4. The method according claim 3 wherein the ionic liquid has a melting point of less than 100°C.

5. The method according to claim 4 wherein the ionic liquid has a melting point of less than 30°C.

6. The method according to any preceding claim wherein the ionic liquid has essentially no vapor pressure.

7. The method according to claim 6 wherein the ionic liquid has a vapor pressure of less than about 1 mm/Hg at 25°C.

8. The method according to claim 7 wherein the ionic liquid has a vapor pressure of less than about 0.1 mm/Hg at 25°C.

9. The method according to any preceding claim wherein the thermal stability of the ionic liquid is form 150°C to 400° C.

10. The method according to claim 9 wherein the thermal stability of the ionic liquid is from 200° C to 300° C.

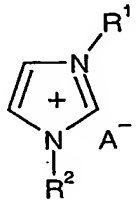
11. The method according to claim 1 or 2 wherein the ionic liquid has a melting point of less than 250°C, a vapor pressure less than about 1mm/Hg at 25°C and the thermal stability of the ionic liquid is from 150° C to 400° C.

12. The method according to any preceding claim wherein the anion of the ionic liquid is selected from the group consisting of Cl^-, Br^-, NO_2^-, NO_3^-, $AlCl_4^-$, BF_4^-,.PF_6^-,CF_3COO^-, $CF_3SO_3^-$, $(CF_3SO_2)_2N^-$, OAc^-, $CuCl_3^-$, $GaBr_4^-$, $GaCl_4^-$, and SbF_6^-.

13. The method according to any preceding claim wherein the cation of the ionic liquid is selected from the group consisting of pyridinium, ammonium, imidazolium, phosphonium, and sulphonium.

14. The method according to any preceding claim wherein the ionic liquid is selected from the group consisting of an imidazolium salt, pyridinium salt, ammonium salt, phosphonium salt, and sulphonium salt.

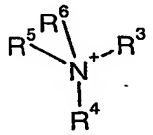
15. The method according to claim 14 wherein the imidazolium salt has formula (I)



(I)

wherein R^1 and R^2 are independently selected from the group consisting of a C_1-C_{18} aliphatic group and a C_4-C_{18} aromatic group; and A^- is an anion.

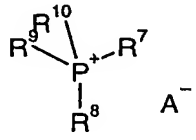
16. The method according to claim 14 wherein the ammonium salt has formula (II)



(II)

wherein R^3, R^4, R^5 and R^6 are independently selected from the group consisting of a C_1-C_{18} aliphatic group and a C_4-C_{18} aromatic group; and A^- is an anion.

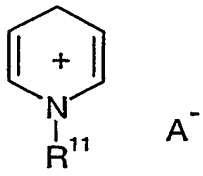
17. The method according to claim 14 wherein the phosphonium salt has formula (III)



(III)

wherein R^7, R^8, R^9 , and R^{10} are independently selected from the group consisting of a C_1-C_{18} aliphatic group and a C_4-C_{18} aromatic group; and A^- is an anion.

18. The method according to claim 14 wherein the pyridinium salt has formula (IV)



(IV)

wherein R^{11} is selected from the group consisting of a C_1-C_{18} aliphatic group and a C_4-C_{18} aromatic group; and A^- is an anion.

19. The method according to any preceding claim wherein the ionic liquid is selected from the group consisting of 1-butyl-3-methylimidazolium hexafluorophosphate, 1-hexyl-3-methylimidazolium hexafluorophosphate, 1-octyl-3-methylimidazolium hexafluorophosphate, 1-decyl-3-methylimidazolium hexafluorophosphate, 1-dodecyl-3-methylimidazolium hexafluorophosphate, 1-ethyl-3-methylimidazolium bis((trifluoromethyl)sulphonyl)amide, 1-hexyl-3-methylimidazolium bis((trifluoromethyl)sulphonyl)amide, 1-hexylpyridinium tetrafluoroborate, 1-octylpyridinium tetrafluoroborate, 1-butyl-3-methylimidazolium tetrafluoroborate, 1-methy-3-ethyl imidazolium chloride, 1-ethyl-3-butyl imidazolium chloride, 1-methy-3-butyl imidazolium chloride, 1-methy-3-butyl imidazolium bromide, 1-methyl-3-propyl imidazolium chloride, 1-methy-3-hexyl imidazolium chloride, 1-methy-3-octyl imidazolium chloride, 1-methy-3-decyl imidazolium chloride, 1-methy-3-dodecyl imidazolium chloride, 1-methy-3-hexadecyl imidazolium chloride, 1-methy-3-octadecyl imidazolium chloride, 1-methy-3-octadecyl imidazolium chloride, ethyl pyridinium bromide, ethyl pyridinium chloride, ethylene pyridinium dibromide, ethylene pyridinium dichloride, butyl pyridinium chloride, benzyl pyridinium bromide, and mixtures thereof.

20. The method according to claim 18 wherein the ionic liquid is selected from the group consisting of 1-octyl-3-methyl-imidazolium hexafluorophosphate, 1-hexyl-3-methy-imidazolium hexafluorophosphate, 1-butyl-3-methyl-imidazolium hexafluorophosphate, 1-butyl-3-methyl-imidazolium tetrafluoroborate, 1-butyl-3-methyl-imidazolium trifluoromethanesulfonate, 1-ethyl-3-methyl-imidazolium trifluoromethanesulfonate, and 1-ethyl-3-methyl-imidazolium bis-(trifluoromethanesulfonyl)-amide.

21. A method to detect volatile components in a sample by headspace gas chromatography, wherein said method comprises dissolving or dispersing a sample in at least one ionic liquid and volatilizing the volatile components of the sample.

22. A method to identify volatile components in a sample by headspace gas chromatography, wherein said method comprises dissolving or dispersing a sample in at least one ionic liquid and volatilizing the volatile components of the sample.

23. A method to quantify volatile components in a sample by headspace gas chromatography, wherein said method comprises dissolving or dispersing a sample in at least one ionic liquid and volatilizing the volatile components of the sample.

24. The method according to any preceding claim wherein the sample is a pharmaceutical compound.

25. A method to detect impurities in a pharmaceutical compound by headspace gas chromatography, wherein said method comprises dissolving or dispersing a pharmaceutical compound in at least one ionic liquid and volatilizing the volatile components of the pharmaceutical compound.